Estimating vitamin D rates among autistic children in Iraq.

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Abstract

This study targeted the 200 children of autism present in the Central Teaching Children's Hospital in the Baghdad governorate, in addition to the cases present in Doctor Haider al-Maliki's clinic that specialized in neurology for children whose age does not exceed 12 years. After obtaining the results, it was found that the percentage of males affected was 84%, while the percentage of females was 16% of the total number of autistic patients. When dividing them according to age groups, the group from 4-6 years appeared 59%, which is considered the most frequent out of the overall number of patients, while the age group from 7-9 years showed 28%. Vitamin D3 level result shows that approximately 15% have a severe D_3 deficiency at rate of 7.6 ng / mL, 50% have deficiency of Vitamin-D in concentrate of 14.2 ng / ml, and 25% have a lack of mild to moderate (Insufficient) at concentration is 23 ng / ml. while in children with autism, the optimal (adequate) level of D3 is 10% and the concentration is 32.6 ng / ml,

In conclusion the rate of concentration of vitamin D_3 for all cases was 17.3 reported as having deficiency of Vitamin-D.

1- Introduction

(ASD)Autism spectrum disorder is an abnormality neurodevelopment which typically occurs in first three years of life. (ASD) are a heterogeneous collection of diverse neurodevelopmental and Behavioral disorders (Moore et al., 2005).

ASD is poorly understood and has no clear therapy, with an uncertain etiology. Over the past decade, the frequency of ASD has risen and is steadily growing. This disorder made the hospital care in front of difficult challenge. It is not clear, though, whether the rise in its incidence is related to diagnostic improvements or even to a real rise in the percentage of conditions (Ashwood et al., 2006). Autism is a category of permanent developmental disorders that are normally not curable, with numerous genetic and environmental risk factors. Autistic adults suffer from poor social contact and verbal and nonverbal communication difficulties. There has been a significant rise in the incidence in recent years. The growth in autism prevalence may not only be attributed to an advancement in diagnosis techniques and the increase in awareness among people (Siegel et al., 1984)

Other neuro-behavior-cognitive disabilities are related with this condition. The signs of this are a broad variety of socio-communication issues, intelligent disability, difficulty speaking, hyperactivity of attention deficit, epilepsy disease, fragile X syndrome, Tuberous sclerosis complex. Furthermore, certain children can also have serious mental illnesses such as depression or disquiet (Gillberg, 2010).

A Ming et al and Gonzalez et al observed the ASDs hquite frequently have a number of biological characteristics. Systemic pathophysiological conditions including elevated oxidative stress, mitochondrial instability and metabolic or immune defects are found among these biological characteristics (Chaste & Leboyer, 2012). In recent years, the interaction between hereditary and environmental parameters has been discovered in ASD. Deficiency of vitamin D has recently been proposed with a possible underlying reason of autism (Coleman & Gillberg, 2012). Deficiency in vitamin D has been recognised as an Epidemiological problem. This deficiency occurs as a result of humans not being exposed to the sun, Which Consider important source of vitamin D for them. The skin produces a hormone that is vitamin D. D3 has hormone-like role of on all bodies tissue. Vitamin D regulates the metabolic pathway of the bones, absorption of calcium, cell differentiation, reproduction and cell death.

Its plays an important role in cancer prevention. Two different compounds are present in vitamin D, including cholecalciferol, that is mainly found in plants, and ergocalciferol, that is essentially found in animals. In order to initiate the synthesis of vitamin D, the skin should be subjected for ultraviolet sunlight, and an activated vitamin-calcitriol form forms just at end(1,25-(OH)2D3) (Braunschweig et al., 2013). Deficiency in vitamin D contributes to osteoporosis, rachitic and osteoarthritis (bone and body pains). In addition, deficiency of vitamin-D plays an important role in several of diseases including multiple sclerosis, spinal arthritis, anxiety, rheumatoid arthritis, autism, crashes, coronary disorders , heart attack, type 1 diabetes, heart rate elevation, crohn's disease, parkinson 's disease, trichomonas vaginalis, chronic migraine, chronic back pain, osteoporosis, asthma, eczema, skin cancer, psoria, Sufficient thyroid Levels improve the immune response and shield people from respiratory infections (Frye et al., 2013). 25(OH)D levels are utilized for each individual to defined the status of vitamin D levels (Meador & Loring, 2013). Vitamin D hormone has been proposed to play an important part in autism because there is a correlation between autism prevalence and low vitamin D levels (Landgren et al., 2010).

Vitamin-D plays a big role in effects of neuro-differentiation, gene control, embryo development, neuroimmunity, antioxidants & antiapoptosis (Idring et al., 2014). (Idring et al., 2014). In patients with autism, a comparatively limited proportion of trials have concentrated on the status of vitamin D. The goal of the current research was to further examine the possible function of Vitamin-D in autism by evaluating vitamin-D 25(OH) rates in kids with Autism.

2. Materials and methods

2-1- The study's location, duration and collection of data

Between March and September 2017, autistic children's blood specimens were obtained of the children in the Children's Central Teaching Hospital and Doctor

Haider AlMaliki's clinic in Baghdad governorate / Iraq which Under his direct oversight.

From each autistic child, 5 ml of venous blood was drawn, placed into a tube, and then a 5,000 rpm centrifuge was used to obtain serum for immunological testing. After being stored in a frozen box to protect the samples, the specimens were transported to the laboratory.

Completed the belongings of the sampling questionnaire on the sex and age of the child.

2-2- Serum 25 (OH) D3 measurement

By using ELISA technique, which is designed to examine and identify human plasma or serum samples, the Serum 25(OH) D3 levels was measured. (Eagle Biosciences Inc., MA, USA).

2- Results and discussion

Autism with gender

The proportion of males to females with autism seen in the findings was 84 percent in boys compared to girls, which were 16 percent in overall cases, as seen in table 3.1.

Gender	Male	Female	Total
Number	168	32	200
Percentage	84%	16%	100

Table (1) ratios of males to females with Autism Spectrum Disorder.

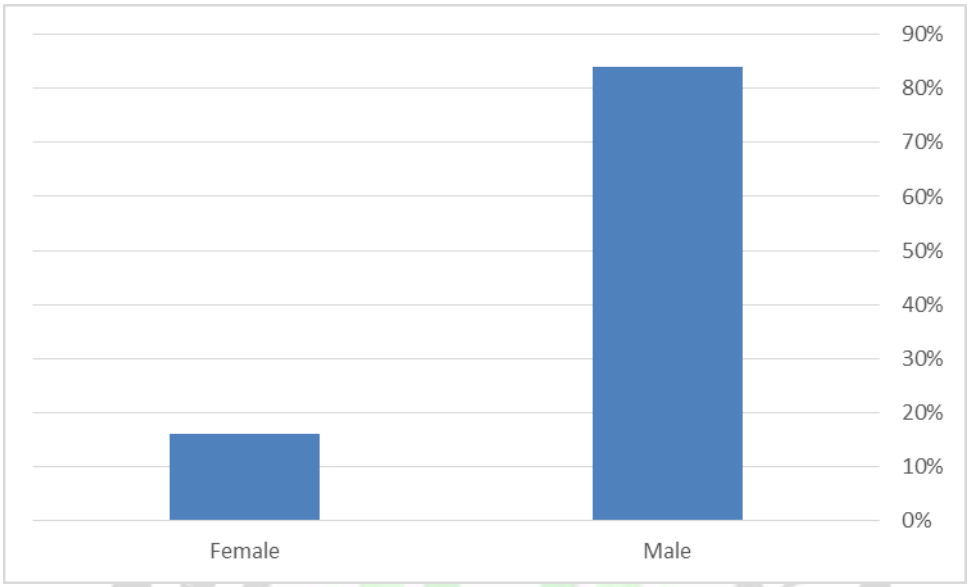

Figure (1) ratios of males to females with Autism Spectrum Disorder

Girls were less likely to be affected than boys, and thus the same finding reached by **Newschaffer *et al*., (2007),**Those Who reported a ratio of gender greater than 5.5: 1, unlike others such as Filipek et al., (1999) observed the gender rate was 4:1. Shao et al. (2002) proposed the autistic is an X-linked condition, which may justify the predominance of autistic in males, while others such as Hallmayer et al. (1996), observable characteristics of male-to-male autistic transmission in families, but excluded X-linkage also as prevalent form of inheritance in all these family members.

In this study 78.2 percent of the children were boys and 21.8 percent were girls.

This distribution of gender is confirmed by ***Sipos et al. (2012)***, which noticed that 73.7% of boys and 26.3% of girls were included in their study, who recorded the autistic is 5 times more likely to appear in males than in females. Of all neurological diseases, the male disparity in the prevalence of autism spectrum disorder is one of the most severe. Developmentally, boys are subjected to testosterone and also its byproduct, estradiol, at elevated amounts. Together all these steroids change the direction of cognitive development by modifying neurogenesis, apoptosis,

proliferation, migration, dendritic and axonal expansion, synaptogenesis and synaptic pruning, both of which may be adversely altered during the path of neuropsychiatric developmental disorders. Several neuroanatomical sexual variations are detected early, starting in utero and progressing to the postnatal age. (Sanders SJ et al.,2015). The primary driver is a rise in estrogen and androgens in the brains of adolescent males as just a result of the fetus testis steroidogenes. Neurogenesis, synaptogenesis and cell differentiation are modulated by steroids by inducing or repressing the expression of genes associated with excitation/inhibition, calcium management and transcription regulators, they are all regulated in ASD. (Baron-Cohen, 2010).

The higher grades of ASD in kids are two sides of the coin. One will be the likelihood of intrinsic risk factors for males that make themselves more prone to gene variant or provocation to the environment. So it seems that it saves girls necessarily from same thing. Studies exploring the biological basis of the gender discrepancy in ASD demonstrate expression level of gonadal steroids in utero (Turner et al., 2015) or accumulated hereditary risk factors of differential penetrance to males versus female. (**Gockley., 2015**). In comparison, multiple studies confirm the argument that before succumbing to ASD, women bear a higher load of gene variation, indicating that they are safe (Robinson et al., 2013) . A third and still untested hypothesis is that women are potentially more vulnerable to hereditary defects that impair brain growth and die in utero disproportionately. (**Jacquemont S., 2014).**

Autism with Age categories

As seen in (Table 3-2), the age category distribution revealed which the 4-6 age category was the most frequently group, at 59 percent of the overall patients, followed by the 7-9 age category at 28 percent.

Freq.	**1-3 years**	**4-6 years**	**7-9 years**	**10-12 years**	**total**
No	8	118	56	18	200
Percentage	4%	59%	28%	9%	100

Table (2) distribution of age categories in ASD.

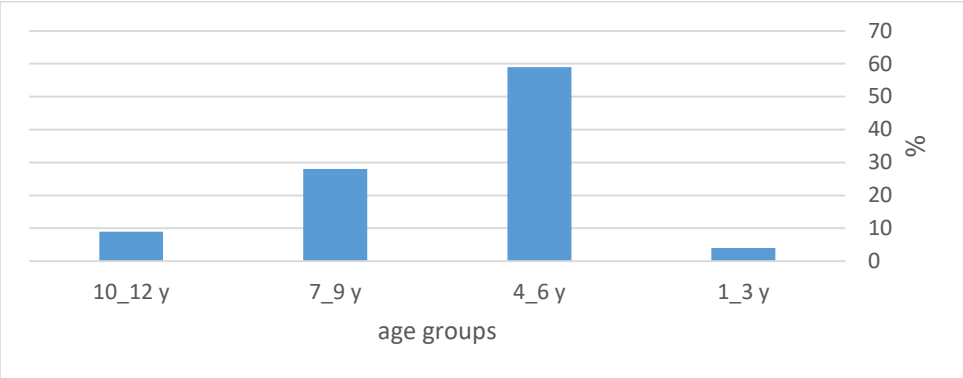

Figure (2) distribution of age categories in ASD

Siblings are usually unable to build a coherent understanding of ASD during the pre-school years, while children as young as three will understand that their sibling with an impairment is something different. Much of the literature on the progress of disease comprehension approaches the developmental processes of the paradigm of Piaget. (**Ko *et al.*, 2004**)

Children in the pre-operative period, according to Piaget, perceive the world according to their direct experience. During that stage, for the production of action and reaction, personal interaction with such interactions is important. This might help illustrate that even young children can understand the physical, but not emotional, disability consequences and causes. (**Burne *et al.*, 2004).**

Many kids have some sort of physical disease before the age of three, which they will later use to refer to others' illnesses. For many of these children, though a sibling with ASD is the first connection they get to an individual that has a "mental illness." Thus, siblings at this period are prone to construct mental impairment explanations to fall within their current schemes. For instance, Becker et al. (2005) requested 3- to 6-year-olds to describe the reasons of different non-physical disorders; physical explanations (e.g., "She fell on her head.")

Kids may also oversimplify their perception of mental disorder to physical disability. for instance, Kids with one study, identified the neurocognitive

deficiencies of children with learning disorders ***(Piven et al., 1995).*** At this age, the absence of illness is still not well known ***(Hardan et al., 2001*)*,*** and pre-schoolers may fear that they may have exposed to or may be able to catch the ASD of their sibling.

Serum 25-Hydroxy Vitamin-D level

In general, (Table.3) indicates Vitamin-D levels. The findings of the present analysis for 200 Iraqi autistic children showed that around 15 percent of them had severe D3 deficiency at a middle point of 7.6 ng/ml whereas 50 percent had vitamin D deficient at a comparison with the reference of 14.2 ng/ml, 25 percent had moderately severe deficiency (insufficient) at a comparison with the reference of 23 ng/ml, while the percentage of acceptable level (sufficient) was 25 percent.

For both patients, the total vitamin D level was 17.3, Which would have classified it as deficiency of Vitamin-D.

Serum 25-Hydroxy Vitamin D in ng/ml	**Vitamin D Status**
≤ 10	Severe Deficiency
10-20	Deficiency
20-30	Mild – Moderate Deficiency
≥ 30	Sufficient
40-50	Ideal
50-150	Indeterminate
>150	Toxicity

Table (3) the range of vitamin D3 level

State level of Vitamin 25(OH)D in ng/ml	Number Of Participants	%	Mean Level Of Vitamin 25(OH)D
Severe Deficiency <10 ng/ml	30	15	7.6
Deficiency 10-20 ng/ml	100	50	14.2
Suboptimal (Insufficient) 20-30 ng/ml	50	25	23.0
Optimal level (Sufficient) ≥ 30 ng/ml	20	10	32.6
Total	100	100	Average mean 17.3

Table (4) the main of vitamin D3 level in Iraqi children have autism

Several reports indicate that 25(OH)D must have a minimum circulation level of more than 30 ng/mL.20-27 Michael Holick cited vitamin D deficiencies as <20 ng/mL and vitamin D ineptitude among 20 and 29 ng/mL (**Holick, 2009**).

Recently, Cannell and Hollis claimed that ideal levels of 25(OH)D must be sustained at 40-70 ng/mL year-round.9 Reinhold Vieth estimated which normal levels,' that is, rates seen in the human living and working in the sun, are about 50 ng/mLL **(Vieth, 2006).**

A team of Australian scientists find in a recent study using laboratory animals that extreme deficiency of Vitamin-D mothers in rats creates offspring with disordered apoptosis and irregular cellular proliferation, in addition to decreased expression of a variety of genes associated in neuronal activity, hyperlocomotion, and memory and learning altered (**Feron *et al.*, 2005).** In addition, a French team discovered that 36 proteins implicated in mammalian brain growth was affected by developmental Vitamin-D deficiency. **(Almeras *et al.*, 2007**). Extreme deficiency of Vitamin-D in pregnancy rat causes structural anomalies similar to those observed with autistic in pups with expanded brain size and swollen ventricular. **(Eyles *et al.*, 2003).** Evidence of continuing systemic inflammation and oxidative stress is seen in the both brain and blood of autistic persons. Autism participants exhibit changes in inflammatory

cytokines, which have been linked with cognitive dysfunction on a regular basis. This inflammatory mediator is close to vitamin D-regulated immune processes. (**Ashwood *et al.*, 2006).** Ensuring proper vitamin D in utero even during childhood to fulfill the transcriptional activity of the vitamin D receptor in the brain could be essential for brain growth as well as for keeping brain abilities later on in life. (**Eyles *et al.*, 2005).** just five kids in this samples had historical background of convulsions of. No statistical significance could be identified, although their mean serum vitamin D levels were relatively lower than the average for those without convulsions. To further explore this point, a much higher sample size is needed.

In this analysis, the number of birth months was defined. The month of June have seen the most childbirth: 18 of the 70 autistic children (25.7%), followed by March and April with 8 newborns each (11.4 percent). Kids were also classified per the birth season. Thirty-three percent of babies were in the summer (33 percent). As the month of June was grouped with summer in this analysis, this is to be predicted. These observations are contrary to other research on autism and birth seasons. Stevens et al. conducted a literature review and noted that at least 7 researchers have discovered excessive autism births in the winter, particularly in March when vitamin D levels are at their lowest levels. **(Stevens et al., 2000)**. levels of Vitamin-D became smallest mostly during summer birth season in the current report, but no descriptive statistics has been identified.

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